

transmembrane conductance regulator) protein wherein said portion consists of between 18 and 100 amino acid residues, wherein 18 amino acid residues of said portion have a sequence as shown in SEQ ID NO: 1.

2. (Twice Amended) The polypeptide of claim 1 wherein the portion of CFTR protein has a 22 amino acid residue sequence as shown in SEQ ID NO: 2.

### **REMARKS**

#### **The Amendments**

Claim 1 has been amended to recite that the polypeptide comprises a portion of the CFTR protein “wherein 18 amino acid residues of said portion have a sequence as shown in SEQ ID NO: 1” in place of “wherein said portion comprises 18 amino acid residues as shown in SEQ ID NO: 1.” This amendment is supported by and clarifies claim 1.

Claim 2 has been amended recite that the portion of the CFTR protein “has a 22 amino acid residue sequence as shown in SEQ ID NO:2” in place of “comprises 22 amino acid residues as shown in SEQ ID NO: 2.” This amendment is supported by and clarifies claim 2.

These amendments merely clarify claims 1 and 2. Thus these amendments introduce no new matter and do not require a new search. These amendments were not made earlier as applicants believed that the amendments and arguments submitted in response to the Office Action dated May 7, 2002 (Paper 10) were sufficient to overcome the rejections. These amendments are also believed to place the claims in condition for allowance. Entry of these amendments is respectfully requested.

### The Rejection of Claims 1 and 2 Under 35 U.S.C. § 102(e)

Claims 1 and 2 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Tsui *et al.*, U.S. Patent 5,776,677. Applicants respectfully traverse.

Claim 1 is directed to an isolated polypeptide comprising a portion of CFTR protein. The portion of CFTR protein consists of between 18 and 100 amino acid residues. Eighteen amino acid residues of the portion have a sequence as shown in SEQ ID NO: 1. Claim 2 recites that 22 amino acid residues of the portion have an amino acid sequence as shown in SEQ ID NO: 2.

To reject claims as anticipated, each element of the claims must be found in a single prior art reference. “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Tsui does not expressly or inherently teach every element as set forth in amended claims 1 and 2.

Tsui teaches the full-length, 1480 amino acid residue sequence of the CFTR protein. (See Tsui at SEQ ID NO: 16.) The final Office Action asserts that Tsui anticipates claims 1 and 2 because the full-length 1480 amino acid residue sequence of CFTR “comprises” SEQ ID NO: 1 or SEQ ID NO: 2. (Paper 12, page 2, line 19 to page 3, line 1.) Claim 1, however, recites a portion of the CFTR polypeptide that “consists of between 18 and 100 amino acid residues.” This is closed language which requires a maximum of 100 amino acids of CFTR. Claim 2 is dependent on claim 1 and therefore also contains this limitation.

Tsui does not teach portions of the CFTR protein that consist of between 18 and 100 amino acids. Tsui teaches the full-length 1480 amino acid sequence of CFTR protein. Thus Tsui

does not each and every element of rejected claims 1 and 2. Withdrawal of this rejection to claims 1 and 2 is respectfully requested.

The Rejection of Claims 3-6 Under 35 U.S.C. § 103(a)

Claims 3-6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Tsui *et al.*, U.S. Patent 5,776,677, in view of Welsh *et al.*, WO 95/25796, and Langel *et al.*, U.S. Patent 6,025,140. Applicants respectfully traverse.

Claim 3 is directed to an isolated polypeptide. The polypeptide comprises a portion of CFTR protein. The portion of CFTR protein consists of between 18 and 100 amino acid residues, has the 18 amino acid residue sequence shown in SEQ ID NO: 1, and is fused to a membrane-penetrating peptide. Claim 4 is directed to an isolated polypeptide like claim 3 with the further recitation that the portion of the CFTR protein has the 22 amino acid residue sequence as shown in SEQ ID NO: 2. Claims 5 and 6 specify that the membrane-penetrating peptide recited in claims 3 and 4 is selected from the group consisting of: VP-22 (SEQ ID NO: 3), (SEQ ID NO: 4), and (SEQ ID NO: 5).

To reject a claim as *prima facie* obvious three criteria must be met:

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) **must teach or suggest all the claim limitations.**

MPEP § 1243; emphasis added. The Patent Office has failed to make a *prima facie* case of obviousness because the combination of Tsui, Welsh, and Langel does not teach or suggest all the limitations recited in claims 3-6.

Tsui is cited as teaching a cystic fibrosis protein comprising the amino acid sequences in SEQ ID NO: 1 and SEQ ID NO: 2. (Paper 10, page 6, lines 7-9.) Welsh is cited as teaching that truncated CFTR polypeptide can be administered alone or in association with an agent that facilitates passage through cell membranes. (Paper 10, page 6, lines 13-15.) Langel is cited as teaching membrane-penetrating peptide sequences that are identical to SEQ ID NO: 4 and SEQ ID NO: 5 of the instant application. (Paper 10, page 6, lines 18-20.) However, none of Tsui, Welsh, or Langel teaches or suggests a portion of CFTR protein that consists of between 18 and 100 amino acid residues wherein 18 amino acid residues of said portion have a sequence as shown in SEQ ID NO: 1 or 22 amino acid residues as shown in SEQ ID NO: 2.

Tsui, discussed above, teaches the full-length 1480 amino acid sequence of human CFTR polypeptide. Tsui does not teach or suggest the recited portions of the CFTR protein.

Welsh does not remedy the defect of Tsui. Welsh teaches truncated CFTR polypeptides. The truncated CFTR polypeptides include at least “the MSD-1, NBD-1 and R domains of CFTR.” (Page 18 of Welsh, lines 22-23.) The MSD-1 domain of the CFTR polypeptide “includes an amino acid sequence that spans from about amino acid residue 76 to residue 360 of CFTR.” (Page 19, line 25 to page 20, line 2.) The NBD-1 domain of CFTR “spans from about amino acid residue 360 to residue 708 of full length CFTR.” (Page 19, lines 17-18.) The R domain of the CFTR polypeptide “includes a 241 amino acid sequence spanning from about amino acid residue 590 to residue 830 of full length CFTR.” (Page 19, lines 9-11.) The

truncated CFTR polypeptides of Welsh thus comprise at least amino acid residues 76 to 830 of CFTR, *i.e.*, at least 755 amino acid residues of CFTR. Welsh does not teach or suggest a CFTR polypeptide that consists of 18 to 100 amino acids as recited in claims 3-6.

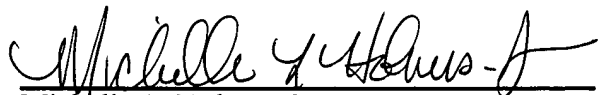
Langel also does not remedy the defect of Tsui. Langel teaches peptides and nucleic acid analogs that are used to transport molecules across lipid membranes. Langel does not teach CFTR polypeptides or portions of CFTR polypeptides. Thus Langel fails to teach or suggest a portion of CFTR that consists of between 18 and 100 amino acid residues as recited in claims 3-6.

The combination of Tsui, Welsh, and Langel does not teach or suggest the recited portions of CFTR protein. Thus the combination fails to teach or suggest all elements of claims 3-6 and the *prima case* of obviousness must fail. Withdrawal of this rejection to claims 3-6 is respectfully requested.

Respectfully submitted,

Date: January 9, 2003

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**Appendix 1. Marked Up Version of the Claims to Show the Changes Made.**

1. (Twice Amended) An isolated polypeptide comprising a portion of CFTR (cystic fibrosis transmembrane conductance regulator) protein wherein said portion consists of between 18 and 100 amino acid residues, wherein [said portion comprises] 18 amino acid residues of said portion have a sequence as shown in SEQ ID NO: 1.
2. (Twice Amended) The polypeptide of claim 1 wherein the portion of CFTR protein [comprises] has a 22 amino acid residue sequence as shown in SEQ ID NO: 2.